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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/244,792	02/05/1999	ALDO T. IACONO	P32130	4164

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EXAMINER	
WANG, SHENGJUN	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/244,792	IACONO, ALDO T.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-37,39,42-45 and 48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-37,39,42-45,48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted November 28, 2005 is acknowledged. Claims 19-37, 39, 42-45 and 48 are pending and are examined.

Claim Rejections 35 U.S.C. 112

a. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 19-37, 39, 42-45 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The recitation of "non-encapsulated cyclosporine" lack support from the application as originally filed. It is recognized the application disclose the genius (cyclosporine in general) and particular species of non-encapsulated cyclosporine (the examples). However, the application lacks a proper written description for the subgenus "non-encapsulated cyclosporine." New or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement. See, e.g., In re Lukach, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); In re Smith, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads). See MPEP 2163.

Claim Rejections 35 U.S.C. 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 19-37, 39, 42-45 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adjei et al. (US 5,635,161), Waldrep et al. (US 5,958,378), in view of Knight et al. (5,049,388), Gordon et al. (US 6,657,893) and Iacono et al. (Am J, Respir. Crit. Care Med. Vol. 155, pp 1690-1698, 1997, IDS)

5. Waldrep et al. and Adjei et al. teaches that cyclosporine are old and well known I combination with various pharmaceutical carriers and excipients in various dosage forms, particularly, aerosol dosage form, wherein the particles size (MMAD) is about 1 to 2 μm. These medicaments are taught as useful for treating graft rejections, inflammation and those conditions herein claimed and disclosed. Specific liposome aerosol dosages are disclosed. See, particularly, the abstract, col. 4, line 22 to col. 5, 64, the examples, col. 13, lines 3-60, and the claims in Waldrep et al. and Col. 1, lines 15-35, and the examples. in Adjei et al. Note, in liposome, the drug is homogeneously distributed among the carrier. Therefore, the carrier, whether be solid (Waldrep et al.) or liquid (Adjei et al.), is considered to be a solvent for the drug. Further, the liposome would not considered as encapsulated since the cyclosporine is homogenously distributed within the carrier, not encapsulated by the carrier.

6. Waldrep et al. and Adjei et al. do not teach expressly the various unencapsulated dosage form, or the dosage levels herein claimed, or the particular time as herein claimed.

7. However, Knight et al. teaches that cyclosporine aerosol dosage may be in the form of powder. See, particularly, example 2 therein. Gordon et al. disclosed that dry powder is a well-known form for pulmonary aerosol drug delivery. See, particularly, col. 1, lines 15-67, and the claims. Aldo et al. teaches a cyclosporine composition for aerosol delivery consisting of cyclosporine, a solvent and a propellant and the method of using the same for treating lung graft rejections. See, the whole article, particularly, page 1691, col. 2, the paragraph subtitled "Drug preparation, aerosol generation, and therapy."

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to treating the patients of organ transplantation within 10 day after the transplantation or prior to the development of symptoms associated the transplant rejection with the aerosol cyclosporine composition herein, or treating other patients who would benefit from the administration of cyclosporine with the aerosol composition herein.

A person of ordinary skill in the art would have been motivated to treating the patients of organ transplantation within 10 day after the transplantation or prior to the development of symptoms associated the transplant rejection with the aerosol cyclosporine composition herein, or treating other patients who would benefit from the administration of cyclosporine with the aerosol composition herein because cyclosporine are known to be useful for organ transplantation patients and are known for treating inflammatory disease herein, and are particularly known to be delivered through pulmonary delivery. Further, the cited prior art as a whole teach various aerosol formulation of cyclosporine, encapsulated, or un-encapsulated as an improvement over simple aerosol employment of powdered active ingredient, and the aerosol cyclosporine as useful for an anti-inflammation, anti-rejection medicaments. The skilled artisan

would have possessed all conventional administration regimens, and seen the selection of one or another as the simple selection from among obvious alternatives. Further, optimization of a result effective parameter, e.g., effective amount of a therapeutical agent, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215. Further, as disclosed in the prior art, the employment of the particular method disclosed therein is to improve the old and well-known aerosol delivery method. Therefore, employ the compound only without the further employment of carrier as herein recited would have been within the purview of the skilled artisan.

Response to the Arguments

Applicants' amendemnts and remarks submitted November 28, 2005 have been fully considered, but are not persuasive.

Applicants assert that the claims are supported in the written description, and argue the claims are supported by the application implicitly. The arguments are untenable. Particularly, it is well settled law that for a situation where only genus and particular species are described, but not the subgenus, there is a lack of written description for the subgenus. See, e.g., In re Lukach, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); In re Smith, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads). See MPEP 2163.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into

account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Particularly, applicants assert that the examiner need a hindsight reconstruction to reach the claimed limitation of "within 10 days following transplantation or prior to the development of symptoms associated with transplant rejection." Particularly, applicants contend that the cited references do not teach such limitation and Iacono particularly, suggest administration well after transplantation. The arguments lack probative force. It is well settled that optimization of a result effective parameter is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215. Therapeutical regimens of a known therapeutical agent are deemed to be results effective parameters. Further, it is well understood that optimization of effective amounts or and administrative regimens in pharmaceutical art is considered within the skill of the artisan. *Ex parte Skuballa* 12 USPQ2d 1570. It is well understood that "wherein the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F. 2d 454, 456, 105 USPQ 233,235 (CCPA 1955). Iacono shows the usefulness of cyclosporine A for treating lung acute rejections. Particularly, Iacono states "the correlation observed between deposition of cyclosporine aerosol and physiological improvement of lung function suggest that there is a dosa-response relationship between the concentration of cyclosporine in allograft and immunologic tolarance." (the abstract). Nowhere in Iacono teaches or suggests that the cyclosporine A had to be used long after the transplantation to be effective. A therapeutical agent known to be effective for treating a disorder, or a symptom

would have been reasonably expected to be useful for a prophylactic treatment of such disorder or symptom.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang
Primary Examiner
Art Unit 1617